

Notice of Allowability**Application No.**

09/465,491

Examiner

Jeanine A Goldberg

Applicant(s)

CHANG ET AL.

Art Unit

1634

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address--

All claims being allowable, PROSECUTION ON THE MERITS IS (OR REMAINS) CLOSED in this application. If not included herewith (or previously mailed), a Notice of Allowance (PTOL-85) or other appropriate communication will be mailed in due course. **THIS NOTICE OF ALLOWABILITY IS NOT A GRANT OF PATENT RIGHTS.** This application is subject to withdrawal from issue at the initiative of the Office or upon petition by the applicant. See 37 CFR 1.313 and MPEP 1308.

1. ☒ This communication is responsive to 2/21/03.
2. ☒ The allowed claim(s) is/are 21,28-30,32,33,35-37,46 and 47.
3. ☒ The drawings filed on 16 December 1999 are accepted by the Examiner.
4. ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
 - a) ☐ All b) ☐ Some* c) ☐ None of the:
 1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this national stage application from the International Bureau (PCT Rule 17.2(a)).
 - * Certified copies not received: _____.
5. ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
 - (a) ☐ The translation of the foreign language provisional application has been received.
6. ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Applicant has THREE MONTHS FROM THE "MAILING DATE" of this communication to file a reply complying with the requirements noted below. Failure to timely comply will result in ABANDONMENT of this application. **THIS THREE-MONTH PERIOD IS NOT EXTENDABLE**

7. ☐ A SUBSTITUTE OATH OR DECLARATION must be submitted. Note the attached EXAMINER'S AMENDMENT or NOTICE OF INFORMAL PATENT APPLICATION (PTO-152) which gives reason(s) why the oath or declaration is deficient.
8. ☐ CORRECTED DRAWINGS must be submitted.
 - (a) ☐ including changes required by the Notice of Draftsperson's Patent Drawing Review (PTO-948) attached
 - 1) ☐ hereto or 2) ☐ to Paper No. _____.
 - (b) ☐ including changes required by the proposed drawing correction filed _____, which has been approved by the Examiner.
 - (c) ☐ including changes required by the attached Examiner's Amendment / Comment or in the Office action of Paper No. _____.

Identifying indicia such as the application number (see 37 CFR 1.84(c)) should be written on the drawings in the front (not the back) of each sheet.

9. ☐ DEPOSIT OF and/or INFORMATION about the deposit of BIOLOGICAL MATERIAL must be submitted. Note the attached Examiner's comment regarding REQUIREMENT FOR THE DEPOSIT OF BIOLOGICAL MATERIAL.

Attachment(s)

- | | |
|--|---|
| 1 <input type="checkbox"/> Notice of References Cited (PTO-892) | 2 <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3 <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 4 <input type="checkbox"/> Interview Summary (PTO-413), Paper No. _____ |
| 5 <input type="checkbox"/> Information Disclosure Statements (PTO-1449), Paper No. _____ | 6 <input type="checkbox"/> Examiner's Amendment/Comment |
| 7 <input type="checkbox"/> Examiner's Comment Regarding Requirement for Deposit of Biological Material | 8 <input checked="" type="checkbox"/> Examiner's Statement of Reasons for Allowance |
| | 9 <input type="checkbox"/> Other |

REASONS FOR ALLOWANCE

1. This action is in response to the after final amendment filed 2/21/03.
2. The following is an examiner's statement of reasons for allowance.

Claims 21, 28-30, 32-33, 35-37, 46-47 are drawn, in part, to methods of identifying the presence of cancerous cells in a human sample by determining the quantity of hTERT mRNA comprising B-region coding sequences in sample and non-cancerous cells using a primer pair within exon 8 and a primer pair either upstream of exon 7 or downstream of exon 8 wherein greater quantity of hTERT mRNA comprising the B-region coding sequence is indicative of cancer cells.

The art teaches the identification of B-deletion and the relationship between quantity of hTERT mRNA and cancerous cells. Kilian teaches the beta deletion in the hTCS1 gene (also referred to as hTERT, see specification pg. 1). Kilian teaches numerous oligonucleotide primers which include HT2356R. HT2356R is located within exon 8 and overlaps the last 7 nucleotides of SEQ ID NO: 4. Kilian does not teach a method of identifying the presence of cancerous cells in a sample.

Hisatomi teaches that levels of hTERT mRNA was investigated with regard to tumor tissue and non-cancerous tissues. The difference of hTERT mRNA level was highly significant between the tumor tissue and the non-cancerous liver tissue (abstract). Moreover, a strong correlation between the levels of hTERT mRNA and that of telomerase activity in HCC was observed (abstract). HTERT mRNA was amplified using primers within exon 3 and 4, a real-time PCR system provided the essential information to quantify the initial target copy number (pg 728, col. 1-2). As seen in

Figure 4, a correlation between the quantification of hTERT mRNA and telomerase activity is provided such that telomerase activity may be assessed from the mRNA of hTERT (limitations of Claim 8). Hisatomi teaches that there were significant correlations between the levels of hTERT mRNA and that of telomerase activity ($r=0.751$) in tumor tissues (abstract).

The response filed June 18, 2001 provides that the claimed methods provide an accurate and reproducible measure of telomerase activity by selectively measuring mRNA that encodes an active hTERT protein. Given the comparison of the results of Example 4 and 5 to results of Hisatomi, the methods of the instant application appear to demonstrate unexpected results in a significantly more accurate measure of telomerase activity. The instant specification teaches the r^2 of over 96% indicates that using the hTERT mRNA as a predictor of telomerase activity provides an accurate measure of telomerase activity (page 36). Example 7 demonstrates that using the TaqMan assay described above, normal tissue and tumor tissue samples were different (page 38-39).

The correlation coefficient= 0.751 of Hisatomi is less of a correlation than with the instant methods which demonstrate a high correlation (correlation coefficient =0.9805) (page 14 of response filed June 18, 2001). The response further asserts that "the primary distinction between the methods is the primers used, the results demonstrate that the improvement results from the primers used" (page 14 of response filed June 18, 2001). Therefore, method claims directed to the unexpected benefits of the primers are allowable over the art.

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3. Any comments considered necessary by applicant must be submitted no later than the payment of the issue fee and, to avoid processing delays, should preferably accompany the issue fee. Such submissions should be clearly labeled "Comments on Statement of Reasons for Allowance."

4. Any inquiry concerning this communication or earlier communications from the examiner should be directed to examiner Jeanine Goldberg whose telephone number is (703) 306-5817. The examiner can normally be reached Monday-Friday from 8:00 a.m. to 5:30 p.m.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Jones, can be reached on (703) 308-1152. The fax number for this Group is (703) 305- 3014.

Any inquiry of a general nature should be directed to the Group receptionist whose telephone number is (703) 308-0196.

J. Goldberg
Jeanine Goldberg
May 29, 2003

Gary Ben Zion
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